Medical Xpress

Analyzing tissue-agnostic therapies for the treatment of primary brain tumors

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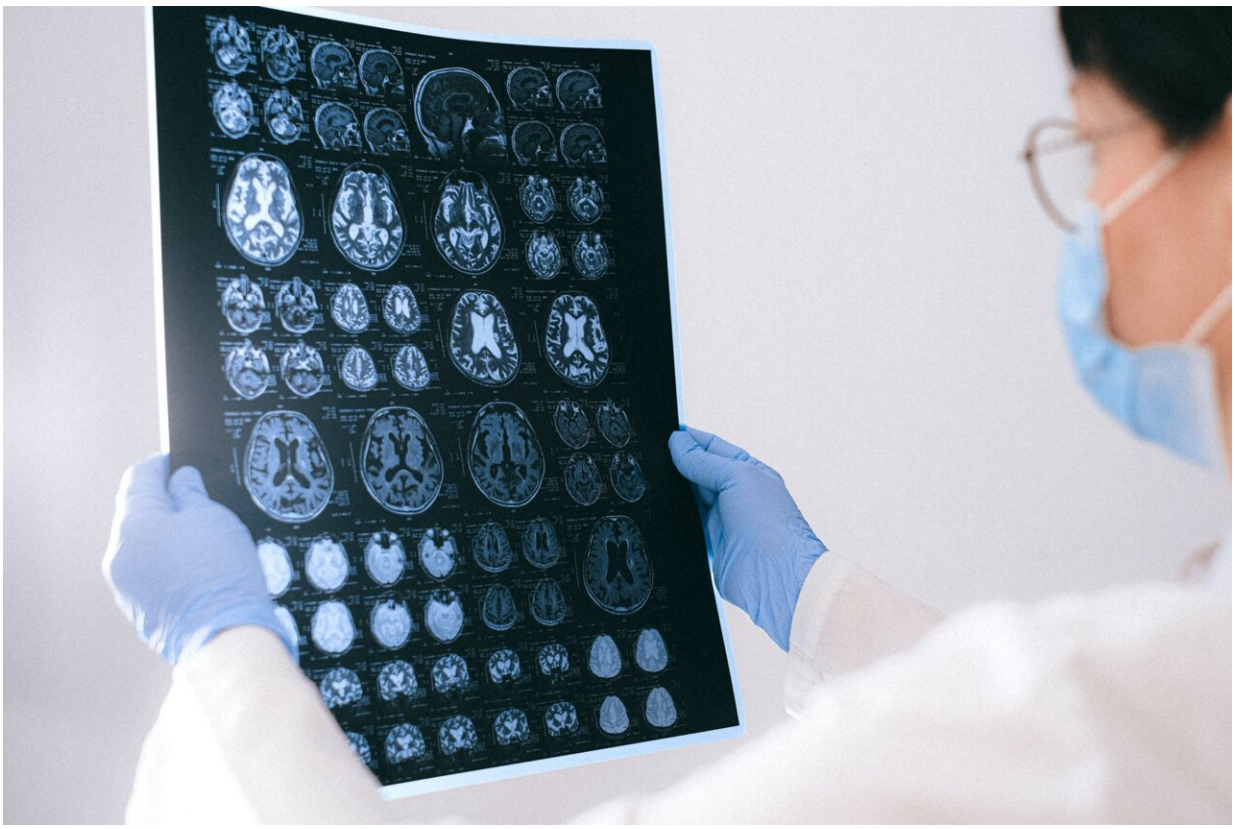

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Researchers from Miami Cancer Institute, part of Baptist Health South Florida, have published a study in *Trends in Cancer* that analyzes the use of tissue-agnostic therapeutics in patients with primary brain tumors

(PBTs). The article describes the current and potential impact of tissue-agnostic therapies on the management of PBTs.

As part of the publication, the researchers discuss data from clinical trials of tissue-agnostic targets for PBTs in the context of challenges in managing these tumors. They also describe additional tissue-agnostic targets that hold promise for benefiting patients with PBTs.

"Novel tissue-agnostic therapeutics targeting driver mutations in tumor cells have been recently approved by the FDA and other regulatory bodies across the world, driven by trials that have demonstrated their efficacy and safety across diverse tumor histology," said Manmeet S. Ahluwalia, M.D., MBA, FASCO, chief of medical oncology, chief scientific officer, deputy director, and Fernandez Family Foundation Endowed Chair in Cancer Research at Miami Cancer Institute, and first author of the study. "However, the relative rarity of primary brain tumors has limited their representation in early trials of tissue-agnostic medications."

Basket trials—which test a targeted therapy on the molecular profiles of a broad spectrum of cancers—have recently led to the next frontier of precision medicine, that is tissue-agnostic approvals. These enable the use of targeted therapies based on molecular alterations that are present regardless of the tissue of origin of the tumor.

There is a substantial genetic, epigenetic, and immunological heterogeneity of PBTs, which adds to the complexity of tissue-agnostic therapies. Innate differences between various types of PBTs must be considered carefully because even within the same tumor, multiple subtypes within the same spectrum can exist, adding to the histological heterogeneity.

However, the concept of tissue-agnostic therapies evolved in the first

place from arguments that common molecular profiles can limit the impact of those inter and intra-tumor heterogeneities from a therapeutic perspective by targeting common molecular alterations.

By gaining a better understanding of tumor biology, several therapeutics with broad efficacy across diverse cancer types have been developed and approved in the last decade. Increasing utilization of next-generation sequencing and biomarker-driven basket trials has helped identify several actionable genetic alterations and their clinical utility. Consequently, this has led to approvals for tissue-agnostic malignancies by the FDA and others, many of which have already demonstrated utility in PBTs.

"However, the limited number of patients with different PBTs in published studies hampers their widespread uptake," added Ahluwalia. "Therefore, it is becoming increasingly crucial for individuals with primary brain tumors to undergo molecular profiling, enabling the maximization of therapeutic options based on individualized characteristics and for real-world analytics to capture this data. These tissue-agnostic approvals, as the new frontier of precision oncology, hold promise for improved treatment outcomes of gliomas."

More information: Manmeet S. Ahluwalia et al, Impact of tissue-agnostic approvals on management of primary brain tumors, *Trends in Cancer* (2024). DOI: 10.1016/j.trecan.2023.11.005

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